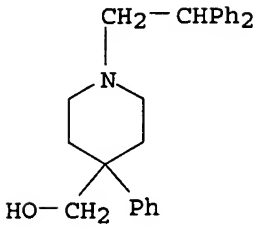
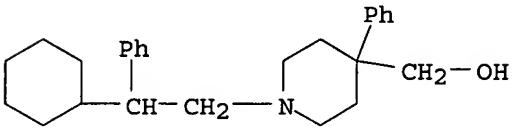
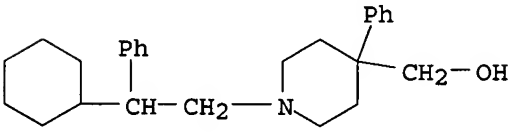


RN 96763-96-1 CAPLUS
CN 4-Piperidinemethanol, 1-(β-cyclohexylphenethyl)-4-phenyl-, hydrochloride (7CI) (CA INDEX NAME)



● HCl

RN 804442-77-1 CAPLUS
CN 4-Piperidinemethanol, 1-(2-cyclohexyl-2-phenylethyl)-4-phenyl- (9CI) (CA INDEX NAME)



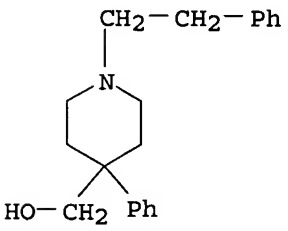
L11 ANSWER 49 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
GI For diagram(s), see printed CA Issue.
AB The title derivs., of general formula (I), in which R was CH2OH, CH(OH)Me, or CH-(OH)Et, A represented a C1 to C6 alkylidene radical, and R' was an alkoxy, a substituted-alkoxy, an aryloxy, an aralkoxy an aryl, an heterocyclic, or a tetrahydrofurfuryloxy radical, were prepared by either the reduction of an appropriate derivative of I (R = an alkoxycarbonyl radical, Ac, or EtCO and A and R' as stated) or the alkylation of a piperidine of general formula (I, AR' = H) (II) [R = CH2OH, CH(OH)Me, or CH(OH)Et] with an halide of type R'AX (III) (X = I, Br, or Cl and R' and A as stated). Thus, 8 parts I (R = CO2Et, A = CH2CH2 R' = 2-tetrahydrofurfuryloxy in 120 parts Et2O added to 1 part LiA1H4 in 120 parts Et2O, the suspension boiled 10 min., cooled, and treated with 75 parts Rochelle salt (as 20% aqueous soln,), the mixture extracted with Et2O, and the Et2O extract evaporated and disd. gave
I (R = CH2OH, A = CH2CH2, R' = 2-tetrahydrofurfuryloxy, b0.05 160°, n20D 1.5303. Similarly prepared were the following I (R, A, R', and m.p. given): CH2OH, CH2CH2CH2CH2, EtO (b0.4 155°, n20D 1.5180), -; CH2OH, CH2, 2-tetrahydrofuryl, 78-80°; CH2OH, CH2CH2, morpholino, 130°; CH2OH, CH2CH2, piperidino, 106°; CH2OH, CH2CH2,

PhOCH2CH2O, 78°; CH2OH, CH2CH2, PhCH2O, 82-4°. Na (10 parts) added in two portions to 10 parts I (R = CO2Et, A = CH2CH2, R' = EtO) in 35 parts EtOH, the solution boiled 30 min., cooled, diluted with H2O (10 vols.), extracted (exhaustively) with Et2O, and the dried Et2O exts. distilled yielded I (R = CH2OH, A = CH2CH2, R' = EtO), m. 103-4°. The hydrogenation of an alc. solution of I (R = EtCO, A = CH2CH2 R' = PhO) in the presence of PtO2 gave I [R = EtCH(OH), A = CH2CH2, R' = PhO];HBr salt, m. 178°. A mixture of 20 parts II [R = EtCH(OH) (IV)], 250 parts pentanol, 5 parts Na2CO3, and 20 parts IV (R' = 2-tetrahydrofuryl, A = CH2, X = Cl), n20D 1.4553, was refluxed 48 hrs., the suspension filtered, and the filtrate distilled to give I [R = EtCH(OH), A = CH2, R' = 2-tetrahydrofuryl], b0.05 170°, n20D 1.5375. A similar alkylation method was used to prepare I (R = CH2OH, A = CH2CH2, R' = Ph), m. 108° and I (R = CH2OH, A = CH2CH2, R' = HOCH2CH2O), b0.2 180-90°. IV, b0.5 10-5°, was prepared by the PtO2-catalyzed reduction of II (R = EtCO), b0.4 135°, n20D 1.5467, and II (R = CH2OH), m. 80°, was obtained by the LiAlH4 reduction of II (R = CO2Et). The I were nonadditive antitussives without pethidine-like analgesic properties.

AN 1962:79391 CAPLUS
DN 56:79391
OREF 56:15490a-f
TI 4-(1-Hydroxyalkyl)-4-phenyl-1-substituted-piperidines
IN Stern, Edward Severin; Watt, Robert L.; Hardy, Denis G.
PA J. F. Macfarlan & Co., Ltd.
DT Patent
LA Unavailable

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 888657		19620131	GB	19580714
US 3108111		1963	US	

IT **63080-12-6**, 4-Piperidinemethanol, 1-phenethyl-4-phenyl- (preparation of)
RN 63080-12-6 CAPLUS
CN 4-Piperidinemethanol, 4-phenyl-1-(2-phenylethyl)- (9CI) (CA INDEX NAME)

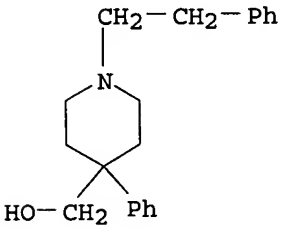


=> d abs bib hitstr 30-39

L11 ANSWER 30 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
GI

with CH2N2, and evidence for oxide by-products has been obtained. 4-Phenylazacycloheptan-4-ols have been made from the azacycloheptanones, and their esterification and dehydration investigated. The ethanolysis and Thorpe-Ziegler cyclization of N-(2-cyanoethyl-)-N-(3-cyanopropyl)benzylamine has been studied. The cyclic product has been shown to have an enaminonitrile structure.

AN 1965:29636 CAPLUS
DN 62:29636
OREF 62:5256a
TI Synthesis and reactions of some azacycloheptan-4-ols
AU Casy, A. F.; Birnbaum, H.
CS Chelsea Coll. Sci. Technol., London
SO Journal of the Chemical Society, Abstracts (1964), (Dec.), 5130-4
CODEN: JCSAAZ; ISSN: 0590-9791
DT Journal
LA English
OS CASREACT 62:29636
IT **1231-52-3**, 4-Piperidinemethanol, 1-phenethyl-4-phenyl-, hydrochloride
(preparation of)
RN 1231-52-3 CAPLUS
CN 4-Piperidinemethanol, 1-phenethyl-4-phenyl-, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L11 ANSWER 48 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
AB cf. CA 59, 13935e. A series of N-substituted derivs. of 4-phenyl-4-carbethoxypiperidine (I) was prepared for pharmacological testing. I (46.6 g., b0.5 140°, m. 36-8°) and 42 g. K2CO3 in 250 ml. anhydrous C6H6 treated, under stirring, dropwise with 31 g. BzCH2Cl (II) in 200 ml. C6H6 in 45 min. at room temperature, the mixture stirred 2 hrs., refluxed 1 hr., kept overnight at room temperature, and worked up gave 63.2 g. 1-phenacyl-4-phenyl-4-carbethoxypiperidine (III), m. 114° (C6H6-petr. ether or 60% EtOH); HCl salt m. 175-80° (Me2CO-EtOH-Et2O). III (15 g.) in 150 ml. anhydrous EtOH, Pd-C (prepared from 3 g. PdCl2), and 0.3 g. PdCl2 hydrogenated under shaking at normal conditions 5 hrs. gave 9.4 g. 1-(2-phenyl-2-hydroxyethyl)-4-phenyl-4-carbethoxypiperidine (IV), m. 128.5° (80° EtOH); HCl salt m. 192° (aqueous EtOH). IV (3 g.), 15 ml. anhydrous C5H5N, and 15 ml. Ac2O kept overnight at room temperature and worked up gave 3.0 g. HCl salt of 1-(2-phenyl-2-acetoxyethyl)-4-phenyl-4-carbethoxypiperidine monohydrate, m. 110-20° and 173-5° (H2O). IV (3 g.), 15 ml. anhydrous C5H5N, and 15 ml. (EtCO)2O gave similarly 3.7 g. HCl salt of 1-(2-phenyl-2-

L11 ANSWER 46 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
GI For diagram(s), see printed CA Issue.
AB The title compds. I, useful as muscle relaxants, were prepared Thus 35 g. AlCl3 was added to 200 ml. PhOPh, 35 g. γ-chlorobutyryl chloride added, and the solution stirred 1 hr. to give p-Cl(CH2)3COC6H4OPh. A mixture of 0.05 mole p-phenoxy-β-chloropropionate, 0.05 mole 4-phenyl-1,2,5,6-tetrahydropyridine, 0.05 mole Et3N, and 25 ml. HCONMe2 was heated at 70 for 4 hrs., poured into H2O, worked up, and 2-naphthalenesulfonic acid in 200 ml. iso-PrOH added to give 16 g. 1-[2-(p-phenoxybenzoyl)ethyl]-4-phenyl-1,2,5,6-tetrahydropyridine 2-naphthalenesulfonate, m. 190.5-91°, which was converted to the free base (II) and then to the hydrochloride, m. 190-1°, by adding excess alc. HCl. Similarly prepared were 1-[γ-(p-phenoxybenzyl)propyl]-4-phenyl-1,2,5,6-tetrahydropyridine 2-naphthalenesulfonate, m. 202-3.5°; HCl salt, m. 163-65°. A mixture of 0.005 mole II, 0.005 mole NH2OH.HCl, and 20 ml EtOH was heated in warm water for 2 hrs. to give II oxime, m. 182-4°. A mixture of 0.01 mole II, 0.05 mole NaBH4, and 150 ml. EtOH was refluxed 6 hrs. to give 65% 1-[3-hydroxy-3-(p-phenoxyphenyl)propyl]-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 203-3.5°. Similarly prepared were 3-[N-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)]-1-[4-(p-nitrophenoxy)phenyl]-1-propanol-HCl, m. 214-15°; N-[4-hydroxy-4-(p-phenoxyphenyl)butyl]-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 160-1°; 3-piperidino-1-(p-phenoxyphenyl)-1-propanol, m. 79-81°; 4-piperidino-1-(p-phenoxyphenyl)-1-butanol-HCl, m. 153-3.5° (iso-PrOH-heptane); 4-(o-methoxyphenyl-1-piperazinyl)-1-(p-phenoxyphenyl)-1-butanol-HCl, m. 199-201°; 3-[N-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)]-1-[4-p-fluorophenoxy)-phenyl]-1-propanol, m. 112-13°. A mixture of 0.05 mole 4-(p-nitrophenoxy)acetophenone, 0.05 mole paraformaldehyde, 0.05 mole 4-phenyl-1,2,5,6-tetrahydropyridine-HCl, and 25 ml. HOAc was stirred at 95° for 2 hrs. The HOAc was evaporated and the residue diluted with acetone to give 11.68 g. 2-[4-(4-nitrophenoxy)benzoyl]ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 198-9°. Similarly prepared were 1-(o-methoxyphenyl)-4-[2-(p-phenoxybenzoyl)ethyl]piperazine-HCl, m. 173-5°; 2-[4-(p-fluorophenoxy)benzoyl]ethyl-4-phenyl-1,2,5,6-tetrahydropyridine-HCl, m. 192-3° (BuOH). A mixture of 0.005 mole 3-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)-1-(p-phenoxyphenyl)-1-propanol, 0.005 mole BuNCO, and 30 ml. toluene was refluxed for 2 hrs., the toluene evaporated, and the residue treated with 0.6 g. fumaric acid (in iso-PrOH) to give 3-(4-phenyl-1,2,5,6-tetrahydro-1-pyridyl)-1-(phenoxyphenyl)-1-propanol N-butylcarbamate fumarate, m. 128-30° (heptane-BuOH). A solution of 0.15 mole piperidine, 0.075 mole p-phenoxy-3-chloropropiophenone, and 30 ml. HCONMe2 was heated at 70° for 4 hrs. and the product treated with 13 g. 2-naphthalenesulfonic acid (in iso-PrOH) to give 11.5 g. β-(N-piperidino)-p-phenoxypropiophenone 2-naphthalenesulfonate, m. 140-3°. The base, m. 168-71°, was liberated from the salt and then converted into the HCl salt, m. 162-3°. A mixture of 0.075 mole piperidine, 0.075 mole γ-chloro-p-phenoxybutyrophenone, 0.075 mole anhydrous K2CO3, 0.075 mole NaI, 30 ml. HCONMe2, and 6.4 g. piperidine was refluxed 24 hrs. and the product treated with 15 g. C10H7SO3H-2 to give 8.4 g. γ-(N-piperidino)-p-phenoxybutyrophenone-C10-H7SO3H-2. Similarly prepared were 1-[γ-(p-phenoxybenzoyl) propyl]-4-hydroxypiperidine, m. 97.5-8.5° (heptane-iso-PrOH), HCl salt m. 104-6°; 1-[γ-(p-phenoxy)benzoylpropyl]-4-(m-trifluoromethylphenyl)-4-hydroxypiperidine-C10H7SO3H-2, m. 161-3° (ios-PrOH); 1-[γ-(p-phenoxybenzoyl)-4-phenyl-4-

hydroxymethylpiperidine-C10H7SO3H-2, m. 129.5-32°; γ-[N-4-(carbethoxy-4-phenylpiperidino)-p-phenoxybutyrophenone]-C10-H7SO3H-2 (number m.p. reported); 1-[γ-(p-phenoxybenzoyl)propyl]-4-(o-methoxyphenyl)piperazine-C10H7SO3H-2, m. 215-17°; HCl salt m. 202-4°. A MeOH solution of 0.004 mole 1-(o-methoxyphenyl)-4-[2-(p-phenoxybenzoyl)ethyl]piperazine was treated with 0.004 mole NaBH4 in 3 portions over 1.5 hrs. to give 1.35 g. 1-(o-methoxyphenyl)-4-(p-phenoxycinnamyl)piperazine-HCl, m. 164.5-5.5°.

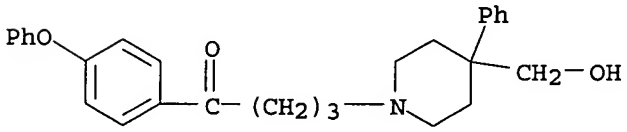
AN 1969:87583 CAPLUS
DN 70:87583
TI N-(p-Phenoxybenzoylalkyl)-4-phenyl-1,2,5,6-tetrahydropyridines and the corresponding alcohols and carbamates
IN Biel, John H.; Hopps, Harvey B.
PA Aldrich Chemical Co., Inc.
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3426036	A	19690204	US 1966-570186	19660804
PRAI US 1966-570186	A	19660804		

IT **22620-52-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 22620-52-6 CAPLUS
CN 2-Naphthalenesulfonic acid, compd. with 4-[4-(hydroxymethyl)-4-phenylpiperidino]-4'-phenoxybutyrophenone (1:1) (8CI) (CA INDEX NAME)

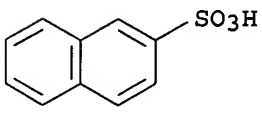
CM 1

CRN 47695-27-2
CMF C28 H31 N O3



CM 2

CRN 120-18-3
CMF C10 H8 O3 S

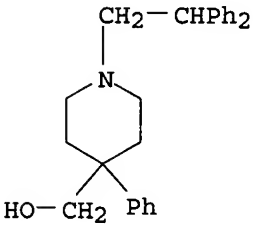


L11 ANSWER 47 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
AB 4-Piperidones have been ring-expanded to azacycloheptanones by reaction

propionoxyethyl)-4-phenyl-4-carbethoxypiperidine, m. 153-5° (Me2CO-EtOHEt2O). I (10 g.) and 3.5 g. anhydrous C5H5N in 50 ml. anhydrous C6H6 treated with 10 g. Ph2CHCOCl (V) in 50 ml. C6H6 under stirring in 30 min., and the mixture kept overnight at room temperature and worked up gave 16.3 g. 1-(diphenylacetyl)-4-phenyl-4-carbethoxypiperidine (VI), m. 94-6° (C6H6-petr. ether). I (10 g.) and 10 g. phenylcyclohexylacetyl chloride (VII) gave similarly 13.5 g. 1-(phenylcyclohexylacetyl)-4-phenyl-4-carbethoxypiperidine (VIII), m. 152-3° (C6H6-petr. ether). VI (10 g.) reduced with 3 g. LiAlH4 in 425 ml. anhydrous Et2O in 5 hrs., and the mixture refluxed 3 hrs. and worked up gave 8.3 g. 1-(2,2-diphenylethyl)-4-phenyl-4-hydroxymethylpiperidine, m. 106-8° (Et2O); HCl salt m. 219-25° (EtOH-Me2CO). VIII (11 g.) gave similarly 8.1 g. 1-(2-phenyl-2-cyclohexylethyl)-4-phenyl-4-hydroxymethylpiperidine, m. 105-6° (anhydrous Et2O); HCl salt m. 168-72° (Me2COEt2O). I (15 g.) and 6.2 g. Cl(CH2)2OH heated 5 hrs. at 100° and worked up gave 13.7 g. 1-(2-hydroxyethyl)-4-phenyl-4-carbethoxypiperidine, b1.5 164-74°, m. 70-80°; HCl salt m. 142-4° (EtOH-Et2O). NaNH2 (9 g.) in 150 ml. anhydrous C6H6 stirred and treated with 12 g. Ph2C(OH)Me, the mixture stirred 20 min. at room temperature, treated with 20 g. HCl salt of 1-(2-chloroethyl)-4-phenyl-4-carbethoxypiperidine (m. 215°), refluxed 7 hrs. with stirring, cooled, decomposed with 150 ml. H2O, the organic layer evaporated in vacuo, and the glassy residue (27.7 g.) chromatographed on 360 g. neutral Al2O3 gave on elution with CHCl3 14 g. 1-[2-(1,1-diphenylethoxy)ethyl]-4-phenyl-4-carbethoxypiperidine, m. 95-6° (C6H6-petr. ether); picrate m. 162° (anhydrous EtOH); methanesulfonate monohydrate m. 84-5° (C6H6-Et2O-petr. ether). I (23.3 g.), 100 ml. iso-AmOH, 9.3 g. anhydrous K2CO3, and 30 g. Me2N(CH2)3Cl refluxed 30 hrs. and worked up gave 11.6 g. 1-(3-dimethylaminopropyl)-4-phenyl-4-carbethoxypiperidine, b1 190°; di-HCl salt hemihydrate m. 240-1° (EtOH); dimethiodide m. 230-2° (EtOH). I (30 g.) and 50 ml. CH2:CHCN kept overnight at room temperature, the mixture treated with 0.5 ml. 50% Et3N(CH2Ph)OH, heated 3 hrs. in a boiling water bath, evaporated in vacuo, and the residue distilled gave 34 g. 1-(2-cyanoethyl)-4-phenyl-4-carbethoxypiperidine (IX), b1 194-8°, m. 51.5° (Et2O-petr. ether); HCl salt m. 193° (Me2CO-EtOH). IX (8 g.) and 1.75 ml. anhydrous EtOH in 15 ml. anhydrous CHCl3 cooled, saturated with anhydrous HCl, and the mixture kept in a closed vessel 2 weeks at room temperature and worked up gave 3 g. di-HCl salt of 3-(4-phenyl-4-carbethoxypiperidino)propionamidine, m. 188-90° (MeOH-Et2O). MeONa (prepared from i g. Na and 10 ml. anhydrous MeOH) treated with 3 g. NH2OH.HCl, the mixture stirred 10 min., filtered, the filtrate treated with 5.72 g. IX in 5 ml. MeOH, and the mixture kept overnight at room temperature and worked up gave 3 g. di-HCl salt of 3-(4-phenyl-4-carbethoxypiperidino) propionamidoxime, m. 172-4° (MeOH-Et2O). I (30 g.) and 50 ml. CH2:CHCO2Et kept 4 hrs. at room temperature, the mixture heated 3 hrs. at 100-10°, evaporated in vacuo, and the residue distilled gave 23.5 g. 1-(2-carbethoxyethyl)-4-phenyl-4-carbethoxypiperidine, b0.6 184-6°; HCl salt m. 147° (Me2CO). I (10.8 g.) in 45 ml. anhydrous Et2O stirred, treated with 3.5 g. CH2:CHAc in 10 ml. Et2O (under reflux), the mixture kept overnight and evaporated, and the residue mixed with petr. ether gave 13.5 g. 1-(3-oxobutyl)-4-phenyl4-carbethoxypiperidine (X), m. 64.5-5.5° (petr. ether); HCl salt m. 147-50° (MeOH-Et2O). X (5.5 g.), 5 g. NH2OH.HCl, 50 ml. EtOH, and 5 ml. C5H5N refluxed 2 hrs. and worked up gave 1-(3-hydroxyiminobutyl)-4-phenyl-4-carbethoxypiperidine, m. 149-52° (EtOH); di-HCl salt m. 129-32° (MeOH-Et2O); methiodide m. 167-9° (EtOH-Et2O). I

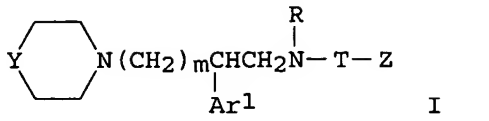
(10 g.) and 5.2 ml. concentrated HCl in 15 ml. H2O heated to 75-80°, the solution stirred, treated dropwise in 45 min. with 3.3 g. NaNO2 in 10 ml. H2O, and the mixture stirred 2 hrs. at 75-80°, kept overnight at room temperature, and worked up gave 11.5 g. 1-nitroso-4-phenyl-4-carbethoxypiperidine (XI), m. 43-5° (Et2O-petr. ether). XI (9 g.) in 100 ml. 75% AcOH stirred at 60°, treated in 1 hr. with 25 g. Zn, and the mixture stirred 2 hrs. at 60°, cooled, filtered, and the filtrate worked up gave 4.5 g. HCl salt of 1-amino-4-phenyl-4-carbethoxypiperidine, m. 173-7° (EtOH-Et2O). The analgesic, antispasmodic, mydriatic, and central depressing activities of the products are tabulated; III is the most active of the series.

AN 1964:30816 CAPLUS
DN 60:30816
OREF 60:5451f-h,5452a-g
TI Synthetic analgesics. V. Synthetic experiments based on 4-phenyl-4-carbethoxypiperidine (norpethidine)
AU Protiva, M.; Jilek, J. O.; Pomykacek, J.; Jirkovsky, I.; Vejdelek, Z. J.
CS Pharm. Res. Inst., Prague
SO Collection of Czechoslovak Chemical Communications (1963), 28, 2627-36
CODEN: CCCCAK; ISSN: 0010-0765
DT Journal
LA Unavailable
IT **96072-68-3**, 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl-, hydrochloride **96072-69-4**, 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl- **96763-96-1**, 4-Piperidinemethanol, 1-(β-cyclohexylphenethyl)-4-phenyl-, hydrochloride **804442-77-1**, 4-Piperidinemethanol, 1-(β-cyclohexylphenethyl)-4-phenyl-
(preparation of)
RN 96072-68-3 CAPLUS
CN 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl-, hydrochloride (7CI) (CA INDEX NAME)

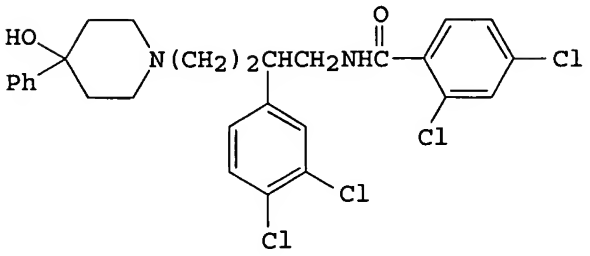


● HCl

RN 96072-69-4 CAPLUS
CN 4-Piperidinemethanol, 1-(2,2-diphenylethyl)-4-phenyl- (7CI) (CA INDEX NAME)



I



II

AB Title compds. I [Y = Cy-N, Ar(CH2)xC(X); Cy = (substituted) Ph, cycloalkyl, pyrimidinyl, pyridyl; Ar = (substituted) Ph, pyridyl, thienyl; x = 0, 1; X = OH, alkoxy, hydroxyalkyl, acyloxy, phenacyloxy, CO2H, carbalkoxy, cyano, aminoalkyl, (di)(alkyl)amino, alkanoylamino, acyl, etc.; m = 2, 3; Ar' = (substituted) Ph, (benzo)thienyl, naphthyl, (N-alkyl)indolyl; R = H, alkyl; T = CO, CONH, C(S)NH; Z = H, M, OM; M = alkyl, (substituted) phenylalkyl, pyridylalkyl, (substituted) naphthylalkyl, pyridylthioalkyl, styryl, etc.] were prepared for use as antiasthmatics and bronchodilators. For example, N-[2-(3,4-dichlorophenyl)-4-hydroxybutyl]-2,4-dichlorobenzamide (preparation given) was converted to the mesylate ester by MeSO2Cl, followed by amination with 4-hydroxy-4-phenylpiperidine, chromatog., and salification, to give title compound II as the HCl salt. I displaced [2-125I histidyl]-neurokinin A from NK-2 receptors of rat duodenal membranes with Ki = 0.50-3 nM, and antagonized NK-2 agonist-induced bronchospasm in guinea pigs.

AN 1992:426590 CAPLUS

DN 117:26590

TI Piperidine- and piperazine-containing arylalkylamines, process for their preparation, and pharmaceutical compositions containing them as neurokinin receptor antagonists.

IN Emonds-Alt, Xavier; Goulaouic, Pierre; Proietto, Vincenzo; Van Broeck, Didier

PA Sanofi SA, Fr.

SO Eur. Pat. Appl., 54 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 474561	A1	19920311	EP 1991-402382	19910905
	EP 474561	B1	19981209		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FR 2666335	A1	19920306	FR 1990-11039	19900905
	FR 2666335	B1	19921211		
	FR 2678267	A1	19921231	FR 1991-7824	19910625
	FR 2678267	B1	19940204		
	IL 99320	A1	19950731	IL 1991-99320	19910827
	AU 9183542	A1	19920312	AU 1991-83542	19910903
	AU 657272	B2	19950309		
	BR 9103802	A	19920519	BR 1991-3802	19910903
	CA 2050639	AA	19920306	CA 1991-2050639	19910904

	CA 2050639	C	19971202		
	FI 9104174	A	19920306	FI 1991-4174	19910904
	FI 98457	B	19970314		
	FI 98457	C	19970625		
	NO 9103469	A	19920306	NO 1991-3469	19910904
	NO 177226	B	19950502		
	NO 177226	C	19950809		
	HU 59098	A2	19920428	HU 1991-2863	19910904
	ZA 9107017	A	19921230	ZA 1991-7017	19910904
	PL 167994	B1	19951230	PL 1991-291618	19910904
	RU 2070196	C1	19961210	RU 1991-5001435	19910904
	JP 04261155	A2	19920917	JP 1991-254730	19910905
	US 5236921	A	19930817	US 1991-755454	19910905
	AT 174332	E	19981215	AT 1991-402382	19910905
	ES 2127722	T3	19990501	ES 1991-402382	19910905
	CZ 285994	B6	19991215	CZ 1991-2724	19910905
	LV 10606	B	19960420	LV 1993-139	19930225
	LT 3442	B	19951025	LT 1993-585	19930531
	US 5350852	A	19940927	US 1993-105677	19930813
	HK 1005290	A1	20000818	HK 1998-104394	19980521
PRAI	FR 1990-11039	A	19900905		
	FR 1991-7824	A	19910625		
	US 1991-755454	A3	19910905		

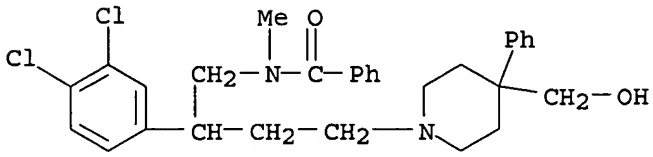
OS MARPAT 117:26590

IT **142001-40-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as neurokinin receptor antagonist)

RN 142001-40-9 CAPLUS

CN Benzamide, N-[2-(3,4-dichlorophenyl)-4-[4-(hydroxymethyl)-4-phenyl-1-piperidinyl]butyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



L11 ANSWER 31 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

GI For diagram(s), see printed CA Issue.

AB The title compds. I [R = dichlorophenyl, nitrocyclohexylphenyl; X = CH:NCH:CH, CH2CH2N(C6H4OMe-o)CH2CH2, CH2CH2CR1R2CH2CH2 where R1 = H, Ph, 2-chlorophenyl, 3-pyrridyl, R2 = H, CH2OH, CO2Et, CONH2, etc.; X1 = CO, CHOH, O] were prepared Thus, a mixture of 14.1 g 4-(hydroxymethyl)-4-phenylpiperidine HCl, 46.8 g 2,6-dichloroacetophenone (II), 2.75 g paraformaldehyde, and 60 mL EtOH containing 0.5 mL concentrated HCl was refluxed for 24 h., 23.5 g II and 2.75 g formaldehyde were added, and the resulting mixture was refluxed for 89 h to give 6.00 g I [R = 2,6-Cl2C6H3, X = CH2CH2CPh(CH2OH)CH2CH2, X1=CO] HCl. I had antifungal activity at 1.5625 μg/mL concentration and analgesic activity at 32-500 mg/kg in mice.

AN 1984:591709 CAPLUS

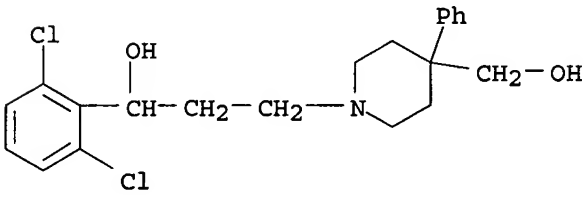
DN 101:191709
TI 1-(2,6-Dichlorobenzoylethyl)-4-(hydroxymethyl)-4-phenylpiperidine and its analogs
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 59106460	A2	19840620	JP 1982-217335	19821210
PRAI JP 1982-217335		19821210		

IT **92823-90-0P 92878-25-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activities of)
RN 92823-90-0 CAPLUS
CN 1-Piperidinepropanol, α-(2,6-dichlorophenyl)-4-(hydroxymethyl)-4-phenyl-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

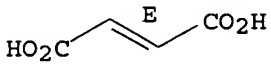
CRN 92823-89-7
CMF C21 H25 Cl2 N O2



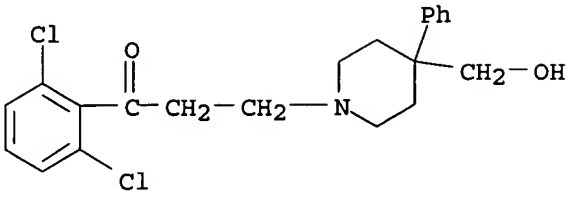
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

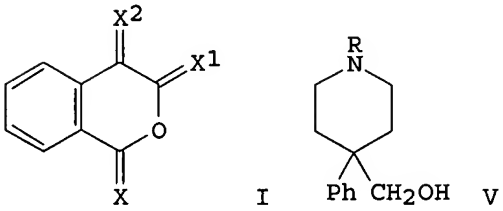


RN 92878-25-6 CAPLUS
CN 1-Propanone, 1-(2,6-dichlorophenyl)-3-[4-(hydroxymethyl)-4-phenyl-1-piperidinyl]-, hydrochloride (9CI) (CA INDEX NAME)



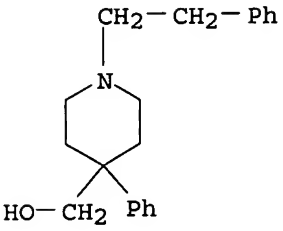
● HCl

L11 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
GI

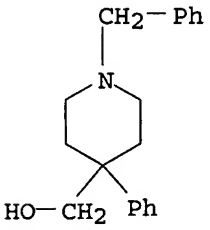


I V

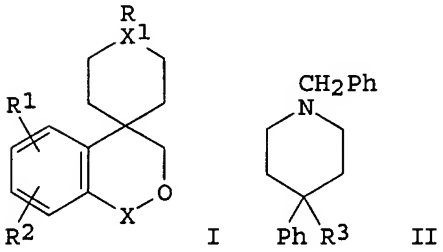
AB Spiro[isochroman-3,4'-piperidin]-1-ones I [X = O, X1 = CH2CH2NRCH2CH2, X2 = H2 (II); X = O, X1 = H2, X2 = CH2CH2NRCH2CH2 (III); (X = X1 = H2, X2 = CH2CH2NRCH2CH2 (IV) (R = Me, PhCH2, PhCH2CH2)] were prepared, e.g. from V, and their analgesic activities were determined III, IV and V had analgesic activity at potent as aminopyrine, whereas II were inactive. Several of the compds. inhibited the histamine release induced by compound 48/80 from isolated rat peritoneal mast cells.
AN 1981:192086 CAPLUS
DN 94:192086
TI Synthesis and biological activity of spiro[isocoumarin-piperidines] and related compounds. I
AU Yamato, Masatoshi; Hashigaki, Kuniko; Ikeda, Masao; Ohtake, Hidetoshi; Tasaka, Kenji
CS Fac. Pharm. Sci., Okayama Univ., Okayama, 700, Japan
SO Chemical & Pharmaceutical Bulletin (1981), 29(2), 402-5
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
OS CASREACT 94:192086
IT **63080-12-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(analgesic and antihistaminic activities of)
RN 63080-12-6 CAPLUS
CN 4-Piperidinemethanol, 4-phenyl-1-(2-phenylethyl)- (9CI) (CA INDEX NAME)



IT **59083-36-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation reaction of, with paraformaldehyde)
RN 59083-36-2 CAPLUS
CN 4-Piperidinemethanol, 4-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L11 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
GI



I II

AB Spiroisochromans I (R = H, alkyl, aralkyl; R1, R2 = H, alkoxy, hydroxyalkyl; X = CH2, CO; X1 = N, CH) were prepared Thus, methanolysis of 5.5 g II (R3 = CN) gave 3.3 g II (R3 = CO2Me), which was reduced quant. to II (R3 = CH2OH). Treating 4 g II (R3 = CH2OH) with (CH2O)n, followed by HCl gave 2.1 g I.HCl (R = benzyl, R1 = R2 = H, X = CH2, X1 = N). The latter compound showed 50% inhibition of histamine release in rats at 6.7 + 10-4 mol/L in vitro.
AN 1981:121329 CAPLUS
DN 94:121329
TI Spiroisochroman
PA Daiichi Seiyaku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 55139381	A2	19801031	JP 1979-45167	19790413
	JP 63006549	B4	19880210		
PRAI	JP 1979-45167	A	19790413		

OS CASREACT 94:121329

IT **59083-36-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and cyclocondensation of, with paraformaldehyde)

RN 59083-36-2 CAPLUS

CN 4-Piperidinemethanol, 4-phenyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)